

CLAIMS

1. A method for identifying a substance capable of disrupting an interaction between (i) a herpes simplex virus (HSV) ICP34.5 polypeptide or a homologue thereof, or a derivative thereof, and (ii) proliferating cell nuclear antigen (PCNA) or a homologue thereof, or a derivative thereof, which method comprises:
- (a) providing an HSV ICP34.5 polypeptide or a homologue thereof, or a derivative thereof, as a first component;
 - (b) providing PCNA, or a homologue thereof, or a derivatives thereof, as a second component;
 - (c) contacting the two components with a substance to be tested under conditions that would permit the two components to interact in the absence of the said substance; and
 - (d) determining whether the said substance disrupts the interaction between the first and second components.
2. A method according to claim 1 wherein the first component is selected from the 63 amino acid C-terminus of ICP34.5 or a derivative thereof, MyD116 and GADD34.
3. A method according to claim 1 or 2 further comprising:
- (e) administering a said substance which has been determined to disrupt the interaction between the first and second components to a mammalian cell; and
 - (f) determining the effect of the said substance on the cell cycle of the said cell.
4. A method according to claim 3, wherein the ability of the said substance to induce cell cycle arrest is determined.
5. A method according to claim 3, wherein the ability of the said substance to induce cell death by apoptosis is determined.

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14. A method of regulating the cell cycle in a mammalian cell, which method comprises administering to said cell a substance capable of disrupting an interaction between (i) a herpes simplex virus ICP34.5 polypeptide or a homologue thereof, or a derivative thereof, and (ii) PCNA or a homologue thereof, or a derivative thereof.

15. A method according to claim 14 wherein administration of the said substance induces growth arrest and/or cell death.

16. A method according to claim 15 wherein said mammalian cell is a tumour cell.

17. A method according to claim 14 wherein administration of the said substance prevents cell death.

18. A method according to claim 17 wherein said mammalian cell is a cell of the central or peripheral nervous system.

19. A human GADD34 homologue which has the following features:

- (i) a molecular mass of approximately 70 kDa as determined by SDS-PAGE;
- (ii) a conserved region which is cross-reactive with an anti-ICP34.5 antibody;
- (iii) cross-reactive with anti-GADD34 antibodies;
- (iv) induced in permissive mammalian cells in response to HSV infection;
- (v) not induced in permissive mammalian cells in response to heat shock or UV damage; and
- (vi) not induced in non-permissive mammalian cells in response to HSV infection.

20. A homologue according to claim 19 wherein said conserved region has at least 30% homology with the C-terminal 63 amino acid residues of an HSV ICP34.5 polypeptide.

Add B3

Add B4

Add B2

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